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MACROMOLECULAR RECOGNITION: STRUCTURAL ASPECTS OF THE ORIGIN OF THE GENETIC SYSTEM

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Theoretical simulation of prebiotic chemical processes is an invaluable tool for probing the phenomenon of evolution of life. Using computational and modeling techniques and guided by analogies from present day systems we seek to understand the emergence of genetic apparatus, enzymatic catalysis and protein synthesis under prebiotic conditions. In one possible scenario, the RNA enzymatic reaction plays a key role in the emergence of the self-replicating and offers a clue to the onset of enzymatic catalysis prior to the existence of the protein biosynthetic machinery. Our ultimate goal is to propose a simple RNA segment which contains the specificity and catalytic activity of the contemporary RNA enzyme and which could emerge in a primordial chemical environment. To understand the mechanism of ribozyme catalyzed reactions ab *initio* and semi-empirical (ZINDO) programs were used to investigate the reaction path of transphosphorylation, A special emphasis was placed on the possible catalytic and structural roles played by the coordinated magnesium cation. Both the inline and adjacent mechanisms of transphosphorylation have been studied. Another important aspect of this reaction is the identity of the functional groups which are essential for the acid base catalysis. The structural characteristics of the target helices, particularly a possible role of G•T pair, is under examination by molecular dynamics (MD) simulation technique.

Modeling of the ancestral aminoacyl-tRNA-synthetases (aRS) may provide important clues to the emergence of the genetic code and the protein synthetic machinery. Assuming that the catalytic function evolved before the elements of specific recognition of a particular amino acid we are exploring the minimal structural requirements for the catalysis of tRNA aminoacylation. The molecular modeling system SYBYL was used for this study based on the high resolution crystallographic structures of the present day tyrosyl-adenylate:tyrRS and $tRNA^{Gln}$: ATP:glnRS complexes. The trinucleotide CCA of the 3'-end tRNA is placed into the active site pocket of tyrRS, based on the scheme of interaction between $tRNA^{Gln}$ and glnRS, and upon the stereochemistry of the tyrRS:tRNA:Tyr-AMP transition state. This provides a model of the non-specific recognition of a tRNA's 3'-end by an aRS, which might be similar to that of the ancestral aRS's. In the next step modeling of the interaction of the rest of the acceptor stem of $tRNA^{Tyr}$ with tyrRS is carried out.